

09421971  
STN. Columbus

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FILE 'HOME' ENTERED AT 07:43:29 ON 20 AUG 2001

-> medline biosis embase capplus uspatfull

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE  
The EXPAND command is used to look at the index in a file  
which has an index. This file does not have an index.

-> a chimeric (p) steroid (p) receptor (p) linker (p) dimer?

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE  
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

-> file medline biosis embase caplus uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

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FILE 'USPATFULL' ENTERED AT 07:44:42 ON 20 AUG 2001  
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

↳ chimeric (p) steroid (p) receptor (p) linker (p) dimer?

1 CHIMERIC (P) STEROID (P) RECEPTOR (P) LINKER (P) DIMER?

→ add total inhib kwic

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2001:380609 CAPLUS  
DOCUMENT NUMBER: 135:805  
TITLE: Chimeric proteins containing hormone receptor  
functional entities and methods of their use  
INVENTOR(S): Gage, Fred H.; Suhr, Steven T.; Gil, Elad B.; Senut,  
Marie-Claude C.  
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA  
SOURCE: PCT Int. Appl., 60 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036447	A2	20010525	WO 2000-US41224	20001017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1999-421971	A1 19991020

## PRIORITY APPLN. INFO.:

AB The invention provides **chimeric** proteins having at least two functional protein units, each contg. the **dimerization** domain of a member of the **steroid/thyroid hormone nuclear receptor** superfamily. The **chimeric** proteins can fold under crystn. conditions to form functional entities. The functional entities optionally contain a novel flexible peptide **linker** of variable lengths between at least two of the protein units. In a preferred embodiment, the **linker** is designed to be increased in increments of 12 amino acids each to aid in prepn. of variant **chimeric** proteins. The DNA binding characteristics of the invention functional entities differ from those of wild-type complexes formed between "monomeric" **receptors** and their binding partners. Some functional entities, e.g. **dimers** expressed as fusion proteins, transactivate responsive promoters in a manner similar to wild-type complexes, while others do not promote transactivation and function instead essentially as constitutive repressors. The invention further provides nucleotide sequences encoding the invention **chimeric** proteins, cells contg. such nucleotide sequences, and methods for using the invention **chimeric** proteins to modulate expression of one or more exogenous genes in a subject organism. In addn., isolated protein crystals suitable for x-ray diffraction anal. and methods for obtaining putative ligands for the invention **chimeric** proteins are provided.

=> s chimeric (p) steroid (p) receptor (p) linker

L2 11 CHIMERIC (P) STEROID (P) RECEPTOR (P) LINKER

=> dup rem 123

L23 IS NOT VALID HERE

The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (>).

=> dup rem 12

PROCESSING COMPLETED FOR L2

L3 11 DUP REM L2 (0 DUPLICATES REMOVED)

=> d 13 total ibib kwic

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:380609 CAPLUS

DOCUMENT NUMBER: 135:805

TITLE: Chimeric proteins containing hormone receptor functional entities and methods of their use  
INVENTOR(S): Gage, Fred H.; Suhr, Steven T.; Gil, Elad B.; Senut, Marie-Claude C.

PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA  
 SOURCE: PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036447	A2	20010525	WO 2000-US41224	20001017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 1999-421971 A1 19991020				

PRIORITY APPLN. INFO.:

AB The invention provides **chimeric** proteins having at least two functional protein units, each contg. the dimerization domain of a member of the **steroid/thyroid hormone nuclear receptor** superfamily. The **chimeric** proteins can fold under crystn. conditions to form functional entities. The functional entities optionally contain a novel flexible peptide **linker** of variable lengths between at least two of the protein units. In a preferred embodiment, the **linker** is designed to be increased in increments of 12 amino acids each to aid in prepn. of variant **chimeric** proteins. The DNA binding characteristics of the invention functional entities differ from those of wild-type complexes formed between "monomeric" **receptors** and their binding partners. Some functional entities, e.g. dimers expressed as fusion proteins, transactivate responsive promoters in a manner similar to wild-type complexes, while others do not promote transactivation and function instead essentially as constitutive repressors. The invention further provides nucleotide sequences encoding the invention **chimeric** proteins, cells contg. such nucleotide sequences, and methods for using the invention **chimeric** proteins to modulate expression of one or more exogenous genes in a subject organism. In addn., isolated protein crystals suitable for x-ray diffraction anal. and methods for obtaining putative ligands for the invention **chimeric** proteins are provided.

L3 ANSWER 2 OF 11 USPATFULL

ACCESSION NUMBER: 2000:174415 USPATFULL  
 TITLE: Regulated transcription of targeted genes and other biological events  
 INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
 Schreiber, Stuart L., Cambridge, MA, United States  
 Spencer, David M., Los Altos, CA, United States  
 Wandless, Thomas J., Cambridge, MA, United States  
 Belshaw, Peter, Cambridge, MA, United States  
 Board of Trustees of Leland Stanford Jr. University, Stanford, CA, United States (U.S. corporation)  
 President and Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)

PATENT ASSIGNEE(S):

PATENT INFORMATION:	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165787		20001226
APPLICATION INFO.:	US 1998-87647		19980529 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-478386, filed on 7 Jun		
	1995, now patented, Pat. No. US 5830462 And a		

continuation-in-part of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266

which

is a continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned , said Ser. No. US

478386

which is a division of Ser. No. US 1995-388653, filed on 14 Feb 1995, now patented, Pat. No. US 5869337

which

is a continuation-in-part of Ser. No. US 1994-196043, filed on 11 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Elliott, George C.

ASSISTANT EXAMINER:

Schwartzman, Robert

LEGAL REPRESENTATIVE:

Berstein, David L., Hausdorff, Sharon F., Clauss, Isabelle M.

NUMBER OF CLAIMS:

129

EXEMPLARY CLAIM:

62

NUMBER OF DRAWINGS:

36 Drawing Figure(s); 36 Drawing Page(s)

LINE COUNT:

5058

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1) -rbm.sub.(n) are **receptor** binding moieties which may be the same or different and which are capable of binding to the **chimeric** protein(s). The rbm moieties are covalently attached to a **linker** moiety which is a bi- or multi-functional molecule capable of being covalently linked

("--") to two or more rbm moieties.. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cydosporin-type moiety, a **steroid** or tetracycline.

Cydosporin-type moieties include cydosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or.

. . Kd value below about 10.sup.-6 M. In some embodiments it is preferred that the ligand bind to a naturally occurring **receptor** with a Kd value greater than about 10.sup.-6 M and more preferably greater than about 10.sup.-5 M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified **receptor** or

**chimeric** molecule containing a modified **receptor**

domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude

less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties

as a C2-C20 alkylene, . . .

L3 ANSWER 3 OF 11 USPATFULL

ACCESSION NUMBER: 2000:50686 USPATFULL

TITLE: Regulated apoptosis

INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States

Schreiber, Stuart L., Cambridge, MA, United States

Spencer, David M., Los Altos, CA, United States

Wandless, Thomas J., Cambridge, MA, United States

Belshaw, Peter, Cambridge, MA, United States

PATENT ASSIGNEE(S): Board of Trustees of Leland S. Stanford Jr. Univ.,

Stanford, CA, United States (U.S. corporation)  
President & Fellows of Harvard College, Cambridge, MA,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6054436		20000425
APPLICATION INFO.:	US 1998-87811		19980529 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266 which is a continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned And a continuation-in-part of Ser. No. US 1994-196043, filed on 14 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Elliott, George C.		
ASSISTANT EXAMINER:	Schwartzman, Robert		
LEGAL REPRESENTATIVE:	Berstein, David L., Hausdorff, Sharon F., Clauss, Isabelle M.		
NUMBER OF CLAIMS:	64		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	35 Drawing Figure(s); 34 Drawing Page(s)		
LINE COUNT:	5061		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1) -rbm.sub.(n) are receptor binding moieties which may be the same or different and which are capable of binding to the chimeric protein(s). The rbm moieties are covalently attached to a linker moiety which is a bi- or multi-functional molecule capable of being covalently linked			
(" -") to two or more rbm moieties.. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a steroid or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or. . . Kd value below about 10.sup.-6 M. In some embodiments it is preferred that the ligand bind to a naturally occurring receptor with a Kd value greater than about 10.sup.-6 M and more preferably greater than about 10.sup.-5 M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified receptor or chimeric molecule containing a modified receptor domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring receptor protein. Linker moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .			
L3 ANSWER 4 OF 11 USPATFULL			
ACCESSION NUMBER:	2000:40892 USPATFULL		
TITLE:	Regulated transcription of targeted genes and other biological events		
INVENTOR(S):	Crabtree, Gerald R., Woodside, CA, United States Schreiber, Stuart L., Cambridge, MA, United States		

PATENT ASSIGNEE(S):  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Belshaw, Peter, Cambridge, MA, United States  
Ho, Steffan N., San Diego, CA, United States  
Board of Trustees of Leland Stanford Jr. University,  
Stanford, CA, United States (U.S. corporation)  
President and Fellows of Harvard College, Cambridge,  
MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6046047		20000404
APPLICATION INFO.:	US 1998-157230		19980916 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-388653, filed on 14 Feb 1995, now patented, Pat. No. US 5869337 And a continuation-in-part of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266		

which

is a continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned , said Ser. No. US

388653

which is a continuation-in-part of Ser. No. US 1994-196043, filed on 14 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Degen, Nancy  
ASSISTANT EXAMINER: Schwartzman, Robert  
LEGAL REPRESENTATIVE: Berstein, David L., Vincent, Matthew P., Clauss, Isabelle M.

NUMBER OF CLAIMS: 127  
EXEMPLARY CLAIM: 65  
NUMBER OF DRAWINGS: 37 Drawing Figure(s); 36 Drawing Page(s)  
LINE COUNT: 4582

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1) -rbm.sub.(n) are **receptor** binding moieties which may be the same or different and which are capable of binding to the **chimeric** protein(s). The rbm moieties are covalently attached to a **linker** moiety which is a bi- or multi-functional molecule capable of being covalently linked

("--") to two or more rbm moieties. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a **steroid** or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or. . . Kd value below about 10.<sup>-6</sup> M. In some embodiments it is preferred that the ligand bind to a naturally occurring **receptor** with a Kd value greater than about 10.<sup>-6</sup> M and more preferably greater than about 10.<sup>-5</sup> M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified **receptor** or **chimeric** molecule containing a modified **receptor** domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties

as a C2-C20 alkylene, . . .

L3 ANSWER 5 OF 11 USPATFULL

ACCESSION NUMBER: 2000:37639 USPATFULL  
TITLE: Regulated transcription of targeted genes and other biological events  
INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
Schreiber, Stuart L., Cambridge, MA, United States  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Ho, Steffan N., San Diego, CA, United States  
Belshaw, Peter, Cambridge, MA, United States  
PATENT ASSIGNEE(S): Board of Trustees of Leland Stanford Jr. Univ.,  
Stanford, CA, United States (U.S. corporation)  
President & Fellows of Harvard College, Cambridge, MA,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6043082		20000328
APPLICATION INFO.:	US 1998-157753		19980916 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-388653, filed on 14 Feb 1995, now patented, Pat. No. US 5869337 which is a continuation-in-part of Ser. No. US 1994-196043, filed on 14 Feb 1994 which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned And a continuation of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266 which is a continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Elliott, George C.		
ASSISTANT EXAMINER:	Schwartzman, Robert		
LEGAL REPRESENTATIVE:	Berstein, David L., Vincent, Matthew P., Clauss, Isabelle M.		
NUMBER OF CLAIMS:	71		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	37 Drawing Figure(s); 36 Drawing Page(s)		
LINE COUNT:	4828		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
SUMM	wherein n is an integer from 2 to about 5, rbm.sub.(1)- rbm.sub.(n) are receptor binding moieties which may be the same or different and which are capable of binding to the chimeric protein(s). The rbm moieties are covalently attached to a linker moiety which is a bi- or multi-functional molecule capable of being covalently linked ("--") to two or more rbm moieties. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a steroid or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or . . . Kd value below about 10. <sup>-6</sup> M. In some embodiments it is preferred that the ligand bind to a naturally occurring receptor with a Kd value greater than about 10. <sup>-6</sup> M and more preferably greater than about 10. <sup>-5</sup> M. Illustrative ligands of . . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified receptor or chimeric molecule containing a modified receptor domain with a Kd value at least one, and preferably 2, and more		

preferably 3 and even more preferably 4 or 5 or more orders of magnitude

less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .

L3 ANSWER 6 OF 11 USPATFULL

ACCESSION NUMBER: 2000:1861 USPATFULL

TITLE: Regulated transcription of targeted genes and other biological events

INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
Schreiber, Stuart L., Cambridge, MA, United States  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Belshaw, Peter, Cambridge, MA, United States

PATENT ASSIGNEE(S): Board of Trustees of Leland Stanford Jr. University, Stanford, CA, United States (U.S. corporation)  
President and Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6011018		20000104
US 1998-87716		19980529 (9)
Continuation of Ser. No. US 1995-388653, filed on 14 Feb 1995, now patented, Pat. No. US 5869337 which is a continuation-in-part of Ser. No. US 1994-196043, filed on 11 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned And a continuation-in-part of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266		

which

is a continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Elliott, George C.

ASSISTANT EXAMINER:

Schwartzman, Robert

LEGAL REPRESENTATIVE:

Berstein, David L., Hausdorff, Sharon F., Vincent, Matthew P.

NUMBER OF CLAIMS:

70

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

36 Drawing Figure(s); 36 Drawing Page(s)

LINE COUNT:

4687

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1)--rbm.sub.(n) are

**receptor** binding moieties which may be the same or different and which are capable of binding to the **chimeric** protein(s). The rbm moieties are covalently attached to a **linker** moiety which is a bi- or multi-functional molecule capable of being covalently linked

("-") to two or more rbm moieties.. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a **steroid** or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or.

. . . Kd value below about 10.<sup>sup.-6</sup> M. In some embodiments it is preferred that the ligand bind to a naturally occurring **receptor** with a Kd value greater than about 10.<sup>sup.-6</sup> M and more preferably greater than about 10.<sup>sup.-5</sup> M. Illustrative ligands of . . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified **receptor** or **chimeric** molecule containing a modified **receptor** domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .

L3 ANSWER 7 OF 11 USPATFULL

ACCESSION NUMBER: 1999:155696 USPATFULL  
 TITLE: Regulated apoptosis  
 INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
 Schreiber, Stuart L., Cambridge, MA, United States  
 Spencer, David M., Los Altos, CA, United States  
 Wandless, Thomas J., Cambridge, MA, United States  
 Belshaw, Peter, Somerville, MA, United States  
 PATENT ASSIGNEE(S): Board of Trustees of the Leland S. Stanford, Jr.  
 Univ., Stanford, CA, United States (U.S. corporation)  
 President and Fellows of Harvard College, Cambridge,  
 MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5994313		19991130
APPLICATION INFO.:	US 1995-483898		19950607 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-292597, filed on 18 Aug 1994, now patented, Pat. No. US 5834266 which is a continuation-in-part of Ser. No. US 1994-196043, filed on 14 Feb 1994, now abandoned And Ser. No. US 1994-179143, filed on 17 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned , said Ser. No. US 196043 which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Elliott, George C.		
ASSISTANT EXAMINER:	Schwartzman, Robert		
LEGAL REPRESENTATIVE:	Berstein, David L., Hausdorff, Sharon F., Vincent, Matthew P.		
NUMBER OF CLAIMS:	48		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 34 Drawing Page(s)		
LINE COUNT:	4791		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
SUMM	wherein n is an integer from 2 to about 5, rbm. <sub>(1)</sub> -rbm. <sub>(n)</sub> are <b>receptor</b> binding moieties which may be the same or different and which are capable of binding to the <b>chimeric</b> protein(s). The rbm moieties are covalently attached to a <b>linker</b> moiety which is a bi- or multi-functional molecule capable of being covalently linked ("--") to two or more rbm moieties.. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a		

cyclosporin-type moiety, a steroid or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or. . . Kd value below about 10.<sup>sup.-6</sup> M. In some embodiments it is preferred that the ligand bind to a naturally occurring receptor with a Kd value greater than about 10.<sup>sup.-6</sup> M and more preferably greater than about 10.<sup>sup.-5</sup> M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified receptor or chimeric molecule containing a modified receptor domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring receptor protein. Linker moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .

L3 ANSWER 8 OF 11 USPATFULL  
ACCESSION NUMBER: 1999:19001 USPATFULL  
TITLE: Regulated transcription of targeted genes and other biological events  
INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
Schreiber, Stuart L., Cambridge, MA, United States  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Belshaw, Peter, Cambridge, MA, United States  
PATENT ASSIGNEE(S): President and Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)  
Board of Trustees of Leland S. Stanford Jr.  
University, Stanford, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5869337		19990209
APPLICATION INFO.:	US 1995-388653		19950214 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-196043, filed on 11 Feb 1994 And Ser. No. US 1994-292597, filed on		
18	Aug 1994, now patented, Pat. No. US 5834266 , each		
Ser.	No. US which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned , said Ser. No. US 292597		
	which is a continuation-in-part of Ser. No. US 1994-179148, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 17931		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Elliott, George C.		
ASSISTANT EXAMINER:	Schwartzman, Robert		
LEGAL REPRESENTATIVE:	Vincent, Matthew P., Clauss, Isabelle M.Foley, Hoag & Eliot LLP		
NUMBER OF CLAIMS:	165		
EXEMPLARY CLAIM:	85		
NUMBER OF DRAWINGS:	37 Drawing Figure(s); 36 Drawing Page(s)		
LINE COUNT:	4716		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1) -rbm.sub.(n) are **receptor** binding moieties which may be the same or different and which are capable of binding to the **chimeric** protein(s). The rbm moieties are covalently attached to a **linker** moiety which is a bi- or multi-functional molecule capable of being covalently linked

("--") to two or more rbm moieties. . . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a **steroid** or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or. . . Kd value below about 10.sup.-6 M. In some embodiments it is preferred that the ligand bind to a naturally occurring **receptor** with a Kd value greater than about 10.sup.-6 M and more preferably greater than about 10.sup.-5 M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified **receptor** or **chimeric** molecule containing a modified **receptor** domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .

L3 ANSWER 9 OF 11 USPATFULL

ACCESSION NUMBER: 1998:138709 USPATFULL  
TITLE: Regulated apoptosis.  
INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
Schreiber, Stuart L., Cambridge, MA, United States  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Belshaw, Peter, Somerville, MA, United States  
PATENT ASSIGNEE(S): President & Fellows of Harvard College, Cambridge, MA,  
United States (U.S. corporation)  
Board of Trustees of Leland Stanford Jr. University,  
Stanford, CA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 5834266		19981110
US 1994-292597		19940818 (8)
Continuation-in-part of Ser. No. US 1994-179143, filed on 7 Jan 1994, now abandoned And Ser. No. US 1994-179748, filed on 7 Jan 1994 which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned , said Ser. No. US		

179143

which is a continuation-in-part of Ser. No. US 1993-93499, filed on 16 Jul 1993

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Elliott, George C.  
ASSISTANT EXAMINER: Schwartzman, Robert  
LEGAL REPRESENTATIVE: Vincent, Matthew P., Clauss, Isabelle M. Foley, Hoag & Eliot LLP

NUMBER OF CLAIMS: 235  
EXEMPLARY CLAIM: 118  
NUMBER OF DRAWINGS: 35 Drawing Figure(s); 34 Drawing Page(s)

LINE COUNT: 5299

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM wherein n is an integer from 2 to about 5, rbm.sub.(1) --rbm.sub.(n) are

**receptor** binding moieties which may be the same or different and which are capable of binding to the **chimeric** protein(s). The rbm moieties are covalently attached to a **linker** moiety which is a bi- or multi-functional molecule capable of being covalently linked ("--") to two or more rbm moieties. . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a **steroid** or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or . . . Kd value below about 10.<sup>-6</sup> M. In some embodiments it is preferred that the ligand bind to a naturally occurring **receptor** with a Kd value greater than about 10.<sup>-6</sup> M and more preferably greater than about 10.<sup>-5</sup> M. Illustrative ligands of . . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified **receptor** or **chimeric** molecule containing a modified **receptor** domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude less than their Kd values with respect to a naturally occurring **receptor** protein. **Linker** moieties are also described in detail later, but for the sake of illustration, include such moieties as a C2-C20 alkylene, . . .

L3 ANSWER 10 OF 11 USPATFULL  
ACCESSION NUMBER: 1998:134626 USPATFULL  
TITLE: Regulated transcription of targeted genes and other biological events  
INVENTOR(S): Crabtree, Gerald R., Woodside, CA, United States  
Schreiber, Stuart L., Cambridge, MA, United States  
Spencer, David M., Los Altos, CA, United States  
Wandless, Thomas J., Cambridge, MA, United States  
Belshaw, Peter, Cambridge, MA, United States  
PATENT ASSIGNEE(S): President & Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)  
Board of Trustees of Leland S. Stanford, Jr. University, Stanford, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5830462		19981103
APPLICATION INFO.:	US 1995-478386		19950607 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-388653, filed on 14 Feb 1995 And a continuation-in-part of Ser. No. US 1994-292597, filed on 18 Aug 1994 which is a continuation-in-part of Ser. No. US 1994-179748, filed on 7 Jan 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-92977, filed on 16 Jul 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17931, filed on 12 Feb 1993, now abandoned , said Ser. No. US		

388653 which is a continuation-in-part of Ser. No. US 1994-196043, filed on 11 Feb 1994 which is a continuation-in-part of Ser. No. US 179748 which is a continuation-in-part of Ser. No. US 92977 which is a continuation-in-part of Ser. No. US 17931

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Elliott, George C.  
ASSISTANT EXAMINER: Schwartzman, Robert  
LEGAL REPRESENTATIVE: Vincent, Matthew P., Clauss, Isabelle M. Foley, Hoag & Eliot LLP

NUMBER OF CLAIMS: 127  
EXEMPLARY CLAIM: 34  
NUMBER OF DRAWINGS: 37 Drawing Figure(s); 36 Drawing Page(s)  
LINE COUNT: 4581

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM wherein n is an integer from 2 to about 5, rbm(.sub.1)-rbm.sub.(n) are receptor binding moieties which may be the same or different and which are capable of binding to the chimeric protein(s). The rbm moieties are covalently attached to a linker moiety which is a bi- or multi-functional molecule capable of being covalently linked

("--") to two or more rbm moieties. . . . those in which the rbm moieties are the same or different and comprise an FK506-type moiety, a cyclosporin-type moiety, a steroid or tetracycline. Cyclosporin-type moieties include cyclosporin and derivatives thereof which are capable of binding to a cyclophilin, naturally occurring or.

. . . Kd value below about 10.sup.-6 M. In some embodiments it is preferred that the ligand bind to a naturally occurring receptor with a Kd value greater than about 10.sup.-6 M and more preferably greater than about 10.sup.-5 M. Illustrative ligands of. . . of FK506, FK520, rapamycin or a derivative thereof modified at C9, C10 or both, which ligands bind to a modified receptor or

chimeric molecule containing a modified receptor

domain with a Kd value at least one, and preferably 2, and more preferably 3 and even more preferably 4 or 5 or more orders of magnitude

less than their Kd values with respect to a naturally occurring receptor protein. Linker moieties are also described in detail later, but for the sake of illustration, include such moieties

as a C2-C20 alkylene, . . .

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:476304 CAPLUS

DOCUMENT NUMBER: 127:105220

TITLE: Monitoring DNA binding molecules in living cells containing a steroid receptor response element array using a fluorescent chimeric protein of the steroid receptor

INVENTOR(S): Htun, Han; Hager, Gordon L.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services,  
USA;

Htun, Han; Hager, Gordon L.

SOURCE: PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720931	A1	19970612	WO 1996-US19516	19961206
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2239951	AA	19970612	CA 1996-2239951	19961206
AU 9712834	A1	19970627	AU 1997-12834	19961206
PRIORITY APPLN. INFO.:			US 1995-8373	P 19951208
			WO 1996-US19516	W 19961206

AB A method of screening for a compd. that binds to a selected nucleic acid

is provided that comprises contacting a compd. fluorescently labeled by a fluorescent protein with a cell having a plurality of copies of the nucleic acid in an array such that the nucleic acid can be directly detected when bound by fluorescently labeled compd. The location of fluorescence within the cell is detected such that fluorescence aggregated

at the site of the nucleic acid array indicates a compd. that binds to the

selected nucleic acid. In particular compds. such a transcription factor can be screened. Reagents for such method are provided including a mammalian cell having a plurality of **steroid receptor** response elements in an array such that the response element can be directly detected when bound by fluorescently labeled **steroid receptor** and a **chimeric** protein comprising a fluorescent protein fused to a **steroid receptor**. Thus, a **chimeric** protein is constructed comprising a 27-kDa green fluorescent protein (GFP, from Aequorea victoria) and fused by a (Gly-Ala)<sub>5</sub> peptide linker to the N-terminal second residue of rat glucocorticoid **receptor** (GR). Improved fluorescence is achieved by using a GFP variant contg. a serine-65 to threonine substitution, which increases the efficiency of formation of the GFP chromophore, and a GR variant contg. a cysteine-656 to glycine mutation has higher affinity for its ligand than endogenous **receptor**. A mammalian cell line named 3134 was derived by transfection of murine mammary carcinoma line C127 with a plasmid contg. 3 functional segments: (a) the bovine papilloma virus 69% transforming fragment serving as a replicon in mammalian cells; (b) mouse mammary tumor virus (MMTV) LTR is

a

**steroid** responsive promoter and contains the GR binding sites; and (c) the Ha-v-ras gene is a transforming oncogene and serves as a reporter for the MMTV promoter. The MMTV LTRs are organized in a head-to-tail tandem array of .apprx.200 copies, and since each promoter sequence contains 4 GR binding sites, the complete array contains 100 GR binding sites. This cell is used to visualize directly the interaction between the fluorescent, **chimeric** GR and its binding site in chromatin in living cells. The system allows screening for DNA-binding ligands

that

(1) activate gene targeting by **steroid receptor**, (2) activate translocation of the **steroid receptor** to the nucleus, (3) are antagonists or agonists of the **steroid receptor**.

=> log y

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CA SUBSCRIBER PRICE	-1.76	-1.76

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